

The promise of new genetic approaches:

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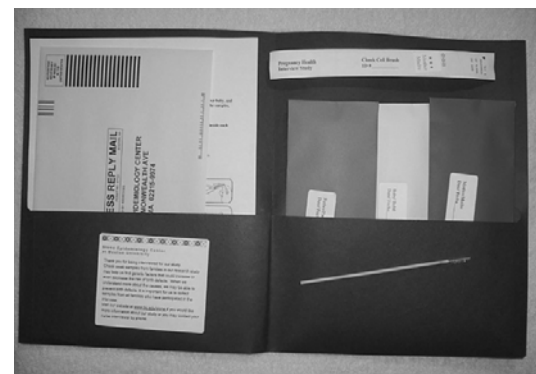


Our study looked at other possible benefits of folic acid on pregnancy. High blood pressure beginning in the second or third trimester (called “gestational hypertension”) can lead to potentially serious complications, including pre-eclampsia or toxemia. Some studies suggest that this might be related to having too much of the amino acid, homocysteine, in the blood. Since folic acid can reduce levels of homocysteine, we wondered if it might lower the risk of gestational hypertension. Indeed, we found that gestational hypertension was lower in women who were taking folic acid supplements around the time of conception. While other studies will need to confirm this finding, it suggests that folic acid may offer even more benefits in pregnancy than we had thought.

A big question women ask is: “Why does my baby have spina bifida when I took folic acid at the time of conception?” When medicines or vitamins affect the risk of birth defects, we know the effect isn’t “all or nothing”. Women who don’t take folic acid don’t all have babies with spina bifida. A likely reason for this is differences in our genetic make-up. A woman with one genetic makeup may metabolize a medicine or vitamin differently from a woman with another genetic makeup—and those differences might be related to the risk of developing high blood pressure in pregnancy or having a baby with a birth defect. It’s for this reason that we ask women to provide cheek swabs from themselves, their baby, and their baby’s father. By studying the different genes that might affect how medicines are handled, we can learn whether certain genetic patterns might be related to birth defects or other complications of pregnancy.

One example of this kind of analysis, involves the risk of gestational hypertension in women who took folic acid around the time of conception. Even though women who took folic acid benefited more than women who didn’t, some women who took folic acid still developed high blood pressure. We know that there are genetic differences in the way women handle folic acid. We tested one of these (called MTHFR 677TT/CT) to see if it might be related to this risk. Among women who did not take folic acid early in pregnancy, we found that a common variation in this gene, in either the mother or fetus, was linked to an increase in the likelihood that the mother would develop high blood pressure.

This finding has to be confirmed in other studies, but it could only have been identified through the willingness of women in our study to provide the cheek cells that are so important. Great strides are being made in our ability to identify how genes affect the way medicines are handled, and this exciting new area of research offers great potential to improve the health of pregnant women and their babies. □



Cheek Cell Kit

New research-Vaccines

Over the years we have looked at many aspects of pregnancy and health. Currently one area of interest is immunizations or vaccines received during or shortly before pregnancy.

Many doctors recommend that pregnant women receive immunizations during pregnancy to protect themselves and the developing fetus. We are trying to learn how many women are vaccinated and which vaccines they have received. If you received a vaccine during your pregnancy, you may be asked to complete a medical record release form so that we can obtain some specific information about it. □

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Pregnancy Health Interview Study News

Slone Epidemiology Center at Boston University

Fall 2006

30 Year Anniversary and Going Strong!

A note from the Principal Investigator

It is hard to believe that we are celebrating our 30th year! We would like to express our deepest appreciation to each of our participating families. We know how busy family life can be and we value the time and effort you took to be part of our research. With your help, we have interviewed over 33,000 women. Thank you!

Although women take a wide variety of medication in pregnancy, we know very little about how those medicines might affect the infant. This lack of information can make a pregnant woman terribly anxious about whether a needed medicine is safe for her baby.

To learn as much as we can,

our study focuses on a wide range of exposures during pregnancy. We consider not only prescription medicines, but also over-the-counter medicines, vitamins, and herbal products. Our study results, which are published in major medical journals, have supported the safety of some products and the risks of others, and as we interview more and more women about their pregnancies, we will have even greater opportunities to answer important questions.

All of us who have devoted our careers to this important public



health effort recognize the generosity of tens of thousands of women who have contributed their experiences to the study. They have consistently told us that by sharing their experiences with us, they are helping to improve the health of future women and their babies. We believe that our scientific contributions over the years show that their participation has and is continuing to make a difference. □

Allen A. Mitchell, MD

Study Nuts and Bolts

The women we interview come from the metropolitan areas of Boston, Philadelphia, Toronto, San Diego and Providence, RI, as well as the state of Delaware, upstate New York and southern New Hampshire. They are mothers of babies with a wide range of birth defects as well as mothers of healthy newborns. We also interview women who have had a pregnancy loss.



We ask questions about many aspects of pregnancy with a special interest in the use of medications and some complications of pregnancy such as prematurity and pregnancy-related high blood pressure. After the interview, all families are invited to provide cheek swab samples which are used to look at

differences in the way women metabolize medications and how these differences may affect fetal development. We also ask each woman to fill out and return a medical record release form. This is very important as it assures that the information we gather about medical diagnoses is complete and accurate and that the results of our study are also accurate.

All information we receive is confidential. We protect the identity of participants by removing all names, addresses, phone numbers and any other identifying information from study data and medical records. Preserving your confidentiality is a priority for us. □

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Pregnancy Health Interview Study Office Staff and Our Interviewers

Study Results

Over the years we have published many articles in medical journals. It would be impossible to list all the study findings here, but we

want to share highlights of a few of them to give you an idea of how your participation will help women and babies in the future. For more

detailed information about our study results please visit our website at www.slone.bu.edu/phis. □

Medicines most commonly taken by pregnant women:

Using data collected over the years, we've looked at which prescription and over-the-counter (OTC) medicines women take in pregnancy. We've also looked at how medication use has changed over the years. In the last 30 years the total number of medicines taken during the first trimester of pregnancy has almost doubled, from

an average of 1.7 in the late 1970's to 3.3 in recent years. Antibiotics are the most common prescription medicines used in pregnancy, taken by about 1 in 12 women. Surprisingly, OTC medicines are taken more often than most prescription drugs. For example, 2 out of 3 pregnant women take acetaminophen, (Tylenol and other

brands) and 1 in 5 take ibuprofen (Advil and others). Many pregnant women take other medicines for colds, headaches, and allergy. We have much to learn about the safety and possible risks of all medicines taken during pregnancy. By learning which ones are taken most often, we can make research on these medicines a priority. □

Exposures that may increase the risk of certain birth defects:

Pregnant women are concerned about exposures that might cause birth defects. Our study has focused on factors that may or may not pose a risk. We know that smoking and alcohol may harm the fetus, but we wondered whether either of these would affect the risk of a specific defect, such as cleft lip and cleft palate. We found that having less than 3 drinks at any one sitting did not seem to be linked to an increased risk of cleft lip or palate. However, 5 or more drinks at a sitting did increase the risk of cleft lip with cleft palate. We also found that smoking in pregnancy was linked to a small increase in the risk of clefts. Even though most smokers don't have babies with clefts, this small increase has now been observed in many other studies, suggesting that smoking is probably involved, though genetic

factors and other exposures may also play a role.

Women's use of antidepressants called "SSRIs" has raised concern about whether these could increase the risk of certain birth defects. About 10 years ago, a study suggested that women who took SSRIs (such as Prozac, Paxil, and Zoloft) in the last half of pregnancy might have an increased risk of having a baby with PPHN, a condition that affects about 1 in 1000 babies who are born with high blood pressure in their lungs that can result in death. The study was too small to be convincing but we felt it was important to see if this risk might be real. In the largest-ever study of PPHN, we found that women who took SSRIs during the last half of pregnancy had a 6-fold increase in the risk of having a baby

with PPHN. However, women who stopped their SSRIs during the first half of pregnancy or took antidepressants that weren't SSRIs didn't have any increase in risk. In the results we published we were careful to point out that this increased risk needs to be kept in perspective. Even if our finding is correct, 99% of babies born to mothers who took SSRIs in late pregnancy would NOT have PPHN. Depression in pregnancy can be a serious problem both for a mother and her baby, and the risk of PPHN is not, in itself, a reason to avoid these medications. Rather, our findings contribute to our understanding about the risks of SSRI medications, and should be considered when women and their health care providers discuss the risks and benefits of using these drugs in pregnancy. □

Exposures which may be safer than we thought:

We often see news reports linking a medicine to birth defects. This causes alarm and raises questions which may be unanswered for years since it takes a long time to conduct a research



study. Because our study is ongoing, we can often answer questions about a particular drug in a relatively short time. For example, in the 1980s there was concern that the anti-nausea drug,

Bendectin, caused birth defects. Using our collected data, we studied Bendectin use and quickly showed that these concerns were without basis. Our findings were supported by almost every other later study that looked at the same question. □

Exposures that may reduce the risk of specific birth defects—the folic acid story:

When our study began 30 years ago, we didn't think that any medicine or vitamin could actually reduce the risk of a birth defect. To our great pleasure, we were wrong. Researchers had suggested that the B-vitamin, folic acid, taken around the time of conception might reduce the risk of a baby being born with neural tube defects, such as spina bifida. We looked at this possibility in our study, and found that women who took a multivitamin containing folic acid around the time of conception reduced the risk of neural tube defects by about half—a dramatic effect, and one that has been shown in most other studies as well. Ours was the first study to show that the amount of folic acid (0.4mg) contained in a standard multivitamin was enough to produce this effect.

Because of the clear benefit of folic acid, we have focused attention on many aspects of it. In other studies, we found that folic acid not only lowers the risk of neural tube defects, but might also lower risks for other birth defects, such as heart

defects, cleft lip and palate, and urinary tract defects.



It's now recommended that women who might become pregnant make sure they take enough folic acid each day, either by eating lots of foods that contain folic acid or by taking a daily multivitamin. There's been some debate over which approach is the best. Getting enough folic acid from a normal diet can be difficult, so the government now requires that this vitamin be added to most flour, corn meal, pasta, and breakfast cereals. We analyzed the diet data we collected and found that even when flour and cereal grains were fortified with folic acid, only about one in five women get the amount they need. For most women,

taking a daily multivitamin that contains folic acid is the better choice.

Next, we looked at our data to see how many women knew about the need for folic acid and how many took a folic acid-containing multivitamin. In the late 1980s, no women knew that folic acid might prevent birth defects—but doctors hadn't learned about those effects, either. By the late 1990's, however, word was getting out, and half the women knew that folic acid could help prevent birth defects. We found that in recent years almost 40% of women take a multivitamin containing folic acid. On the other hand, this means that 60% of women are not taking folic acid. Women with a lower income and less education, along with women who hadn't planned on becoming pregnant, were less likely to know about and take folic acid. This information will help target public education efforts designed to increase the numbers of women taking folic acid around the time of conception. □